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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,119	10/14/2005	Frank-Gerhard Boss	01-2114	5586
28519 7590 04/17/2009 MICHAEL P. MORRIS BOEHRINGER INGELHEIM USA CORPORATION 900 RIDGEBURY RD P O BOX 368 RIDGEFIELD, CT 06877-0368				
EXAMINER ZAREK, PAUL E				
ART UNIT 1617		PAPER NUMBER		
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/525,119

**Applicant(s)**

BOSS ET AL.

**Examiner**

Paul Zarek

**Art Unit**

1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 2/11/2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-3 and 10-22 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 10-22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-8508)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Status of the Claims***

1. Claims 1 and 2 have been amended, Claims 10-22 have been added, and Claims 4-9 have been cancelled by the Applicant in correspondence filed on 02/11/2009. Claims 1-3 and 10-22 are currently pending. This is the second Office Action on the merits of the claim(s).

## **RESPONSE TO ARGUMENTS**

2. The specification was objected to as it being improper to incorporate a website by reference. This objection is withdrawn because Applicants did not attempt to incorporate by reference the subject matter of the website. Examiner notes that Applicants do not intend this URL to be active because it is not placed within these symbols: "<>". The disclosure would be objected to if Applicants intended this URL to be active (MPEP § 608.01(VII)).

3. Claims 2, 3, and 6-7 were rejected under 35 U.S.C. 112, first paragraph, because the specification was not enabled for the prophylaxis of impairments of perception, concentration, cognitive processes, learning and/or memory. Examiner notes that Claims 6 and 7 have been cancelled by Applicant. Amendments to Claim 2 are not sufficient to overcome this rejection. In reply filed on 02/11/2009, Applicants indicate that "the term 'treating' would not generally preclude preventative treatments" (pg 7, lines 14 and 15). In the absence of a definition in the specification, Examiner interprets "treatment" to include "prevention." As discussed in the Office Action mailed on 09/12/2008, the instant specification does not provide enabling

guidance for the prevention of a disease. Therefore, the rejection of Claims 2, 3, and 6-7 were rejected under 35 U.S.C. 112, first paragraph, is maintained.

4. Claims 1-3 were rejected under 35 U.S.C. 103(a) as being unpatentable over in Pickaerts, et al. (above), view of Andreevna, et al. (Journal of Neuroscience, 2001, provided in IDS), Phillips, et al (above). This rejection is moot in light of Applicants' amendments to Claim 1.

5. Claims 1, 2, and 3 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 11, 9, and 10, respectively, of copending Application No. 10/524,956. This rejection is moot in light of the cancellation of Claim 9-11 in the copending '956 application.

6. Claims 1, 2, and 3 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 11 and 12, respectively, of copending Application No. 10/556,437, Claims 13 and 14, respectively, of copending Application No. 10/556,224, and Claims 10, 8, and 9, respectively, of copending Application No. 10/525,115. These rejections are moot in light of Applicants' amendment to Claim 1 of the instant application.

7. Below are listed new grounds of rejection that are not necessitated by amendment to the claims. Therefore, this office action is considered **non-final**. Examiner notes the newly added Claims 20-22. Searching formula (I) or (II) would not constitute an undue search burden. Claims 1-3 and 10-22 are examined below.

***Claim Rejections - 35 USC § 112 (1<sup>st</sup> paragraph)***

8. The text of Title 35, U.S.C. § 112, first paragraph, can be found in a prior Office action.
9. Claims 1-3 and 10-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for improving perception, concentration, cognitive processes, learning, and/or memory comprising administration of formula (I) or (II), or a salt thereof, or the compound of formula (I) or (II), or a salt thereof, does not reasonably provide enablement for said method comprising administering a solvate of formula (I) or (II), or a solvate of the salt of formula (I) or (II), or the solvate or solvate of the salt of formula (I) or (II). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.
10. *In re Wands*, 858 F.2d at 736-40, 8 USPQ2d at 1403-07, set forth eight factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is “undue.” (MPEP § 2164.01(a))
  - a. *The breadth of the claim:* The rejected claims are drawn to a method for improving perception, concentration, cognitive processes, learning, and/or memory comprising administration of formula (I) or (II), or a salt, solvate, or solvate of a salt thereof, or the compound of formula (I) or (II), or a salt, solvate, or solvate of a salt thereof;

- b. *Nature of the invention:* The nature of the invention is a method for improving perception, concentration, cognitive processes, learning, and/or memory comprising administration of formula (I) or (II), or a salt thereof, or the compound of formula (I) or (II), or a salt thereof;
- c. *The state of the prior art:* Approximately one third of drugs are capable of forming crystalline hydrates (Vippagunta, et al., Advanced Drug Delivery Reviews, 2001, pg 15, section 3.1).

Byrn, et al. (Solid State Chemistry of Drugs, 1999), teach that "[t]he occurrence of hydrated or solvated crystal forms, crystals in which solvent molecules occupy regular positions in the crystal structure, is widespread but by no means universal among drug substances." (pg 232, emphasis added). Most drug crystals that fall into the category of solvates are hydrates (pg 236).

Byrn, et al., note that the water molecule is particularly suited to fill structural voids, due to its small size. In hydrated crystal structures, water molecules bind to other water molecules but also to any available functional group, i.e. carbonyls, amines, alcohols, and many others which are capable of accepting or donating an active hydrogen atom to form hydrogen bonds (pg 236, "Hydrates"). The behavior of hydrates of pharmaceuticals is unpredictable due to dehydration prior to melting, and cracking during dehydration (pg 234). Also hydrates and solvates may only be formed under certain conditions, dependent upon the compounds sought to be crystallized. Such a process is not a given in pharmacology and requires a great deal of research, with no reasonable expectation of success.

Furthermore, the stability of solvates and hydrates is not altogether predictable, wherein said stability directly affects the properties of a given molecule. This lack of stability means a hydrate or solvate, if found to possess similar properties as the target compound, may not function as intended, *in vivo*. Such facts lead to the conclusion that more than a mere recitation is needed in order to support a claim to solvates and hydrates. Creating functional solvates and hydrates with the same properties as the mother-compound is by no means routine, thus there must be a showing sufficient to satisfy the enablement requirement;

- d. *Level of one of ordinary skill in the art*: Medicinal chemists would represent an ordinarily skilled artisan. The level of skill would be high;
- e. *Level of predictability in the art*: Just because many drugs are capable of forming hydrates or solvates does not mean that the resulting hydrate or solvate can be predicted before hand. Vippagunta, et al., teach that predicting the formation of solvates or hydrates of a compound is "complex and difficult." "There may be too many possibilities so that no computer programs are currently available for predicting the crystal structures of hydrates and solvates." pg 18, Section 3.4). Byrn, et al., disclose that the properties of solvates and hydrates of a given drug can only be determined empirically;
- f. *Amount of direction provided by the inventor*: Applicants contemplate solvates but provide no guidance for one of ordinary skill in the art to make and use solvates of formula (I) or (II);
- g. *Existence of working examples*: All working examples utilize formula (I) or (II), not the solvate or solvate of the salt thereof; and,

h. *Quantity or experimentation needed to make or use the invention based on the content of the disclosure:* Byrn, et al., and Vippagunta, et al., are explicit in their statements that the formation of solvates or hydrates can not be known without experimentation. Indeed, one of ordinary skill in the art could not ascertain which solvates or hydrates would form with any reasonable expectation of success. The instant specification does not make up for this deficiency, as there is no guidance to an ordinarily skilled artisan to either make a solvate or hydrate of formula (I) or (II). Undue and unpredictable experimentation would be required to use the invention as claimed. Therefore, the instant specification and prior art would not enable one of ordinary skill in the art at the time the invention was made to make and use the invention commensurate with the scope of the rejected claims.

### ***Conclusion***

11. Claims 1-3 and 10-22 are rejected
12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul Zarek whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

/Rita J. Desai/  
Primary Examiner, Art Unit 1625